REMARKS

Applicants submit this response to the Office Action dated January 11, 2007. Claims 1-6, 8-11, and 17-19 are pending. Claims 7, 12-16, and 20-23 are withdrawn pursuant to a restriction requirement. Claims 5, 8, 11, and 17-19 are amended as discussed below, and no new matter is added.

Claims 18 and 19 were rejected under 35 U.S.C. § 112, second paragraph in the Office Action dated April 27, 2006. Applicants assume that since Examiner did not discuss this rejection in the Office Action dated January 11, 2007, applicants' claim amendment filed July 25, 2006 was sufficient to overcome this rejection. If this is not the case, clarification is requested.

Claims 1-4, 8, 10 and 17 were rejected under 35 U.S.C. § 102(e) over McKay et al., U.S. Patent No. 6,455,307. According to the Examiner, McKay discloses an oligonucleotide, SEQ ID NO:93, that corresponds to residues 3435-3452 of applicants' SEQ ID NO:1, including disclosure in a composition comprising pharmaceutically acceptable carriers.

Claim 1, and claims 8 and 17 as amended, recite that the inhibitor, antisense or ribozyme, specifically hybridizes to a polynucleotide encoding Sos1. This is supported in the specification, for example at page 9, lines 1-4, which supports "specific hybridization" of the oligonucleotides to Sos1 DNA or RNA. Specific hybridization would exclude SEQ ID NO:93 of McKay, which would also hybridize with casein kinase 2-alpha. Support is also found in the instant application at page 46, lines 9-11 where applicants describe the specificity of binding of preferred antisense molecules. Applicants state that preferred molecules with the preferred specificity of binding would contain sequences of a general length so as to contain enough sequence to be, "unique among human genes." Clearly the McKay sequence which recognizes at least two sequences among human genes is not "unique" and so would not be contained within the instant application.

Contrary to the Examiner's statement that the disclosure of McKay meets all of the structural requirements of the claimed invention, the oligonucleotide of McKay does not meet the requirement of "specifically hybridizing." In fact, McKay defines antisense

molecules as those that *specifically hybridize* to a target nucleic acid (col. 3, lines 62-65). At col. 5, line 62 to col. 6, line 5, McKay states that an antisense compound is "specifically hybridizable" to a target when non-specific binding to non-target sequences does not occur under appropriate conditions.

Thus, to the extent that residues 3435-3453 of SEQ ID NO:1 herein also bind to the casein kinase 2-alpha of McKay, it would clearly fall outside the definition of an antisense compound for McKay's purposes. Instead, it would be considered by applicants and by McKay as an oligonucleotide not suitable as a specific inhibitor.

The Examiner stated that the oligonucleotide of McKay would specifically hybridize with Sos1 in the absence of a casein kinase 2-alpha mRNA. Applicants strongly disagree with this reasoning and find it illogical. Applicants are claiming molecules that specifically hybridize to their target RNA and not molecules that specifically hybridize to target only in the absence of some other unrelated RNA. The characteristic of "specifically hybridizing" is not a fluctuating trait of an oligonucleotide, dependent on the environment.

The oligonucleotide of McKay might "hybridize" to sequences other than the target, but the art-recognized definition of "specific hybridization" does not include molecules that are capable of hybridizing to two or more unique and unrelated genes. Similarly, the plain and common meaning of the word "specific" is generally thought of as being particular, special or unique. Therefore, the oligonucleotide of McKay does not fall under the claims of the instant application, and reconsideration and withdrawal of this rejection are respectfully requested.

Claims 8, 10, 18 and 19 were rejected under 35 U.S.C. § 102(b) over Schweighoffer, U.S. Patent No. 5,656,595. Schweighoffer allegedly discloses Sos1 inhibitors of SEQ ID NO:5, including antisense molecules for therapeutic purposes.

Schweighoffer fails to disclose any biologically active oligonucleotides of SEQ ID NO:5. Although the reference generally mentions antisense, it fails to show inhibition using an antisense molecule, and it also fails to identify any antisense molecules capable of specifically hybridizing to Sos1 DNA as recited in claim 1. At page 4, lines 12-15 of the Office Action, the Examiner stated that claims 8, 10, 18 and 19 did not recite the "specifically hybridizes" limitation. Claim 8 now depends from claim 1, which

has the limitation; claim 10 depends from claim 8; and claims 18 and 19 have been amended to recite the limitation. Reconsideration and withdrawal of this rejection are respectfully requested.

The Examiner states that Schweighoffer discloses a nucleic acid sequence SEQ ID NO:5 that, "corresponds to the Sos1 sequence of the instant invention [SEQ ID NO:1]." The SEQ ID NO:5 disclosed by Schweighoffer is in fact a partial cDNA sequence and is only 1092 nucleotides in length. SEQ ID NO:1 of the instant invention is the full length sequence of Sos1, and is 3999 nucleotides in length. Clearly the Schweighoffer sequence cannot teach all the applicants' sequence and potential antisense RNAs that could arise from that sequence if only one third of the sequence is disclosed.

In addition, alignment of SEQ ID NO:5 of Schweighoffer with applicants' SEQ ID NO:1 reveals that over the fraction of the Sos1 gene where SEQ ID NO:5 aligns, the sequences only have 71% homology, further demonstrating that Schweighoffer does not anticipate applicants' invention. (Exhibit 1.) Furthermore, the Examiner states, "SEQ ID NOS:2 and 3 are comprised within SEQ ID NO:5." This is simply incorrect. As shown in Exhibit 1, Schweighoffer's SEQ ID NO:5 shows 71% homology with applicants' SEQ ID NO:1 from nucleotides 2190-3054. Applicants' SEQ ID NO:3 corresponds to nucleotides 215- 239 of SEQ ID NO:1, so Schweighoffer's SEQ ID NO:5 clearly cannot contain applicant's SEQ ID NO:3. Applicants' SEQ ID NO:2 corresponds to nucleotides 2469- 2493 of SEQ ID NO:1 (Exhibit 1) and so is roughly contained within Schweighoffer's SEQ ID NO:5, but applicants' SEQ ID NO:2 only shows 80% homology with the corresponding nucleotides of Schweighoffer's sequence (Exhibit 2). Sequences that have only 70-80% homology clearly would not specifically hybridize to applicants' SEQ ID NO:1 as required by claim 1, and so Schweighoffer's sequences are not anticipatory. Applicants respectfully request withdrawal of this rejection.

Claims 1-6, 8-11 and 17-19 were rejected under 35 U.S.C. § 103 over Schweighoffer et al. in view of McKay et al. Applicants have demonstrated that the sequences in McKay fall outside of the claims of the instant invention. Applicants have also demonstrated that the sequence SEQ ID NO:5 disclosed in Schweighoffer is only one third of applicants' sequence SEQ ID NO:1, and that this partial sequence only has

71% homology with applicants' sequence. Furthermore, combining McKay's sequences, which are outside applicants' invention, with Schweighoffer's incomplete and partially homologous sequence does not lead the ordinary worker to applicants' invention. Such a combination would lead that worker to antisense RNAs with only 70% homology with their targets that would hybridize to more that one target sequence. This is not applicants' invention, which specifies antisense oligonucleotides or ribozymes that specifically hybridize to a polynucleotide encoding Sos1.

The Sos1 antisense oligonucleotides disclosed and claimed by the present application cannot be rendered obvious by a reference teaching a sequence that is less than one third of a full length Sos1 sequence. McKay does not supply the missing sequence. There is clearly no case of prima facie obviousness, and applicants respectfully request a withdrawal of this rejection.

If fees are believed necessary, the Commissioner is authorized to charge any required fee, deficiency or credit any overpayment to Deposit Account No. 04-0258. A duplicate copy of this document is enclosed.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

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